EXHIBIT A

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION THIS DOCUMENT RELATES TO ALL WAVE 1 CASES	Master File No. 2:12-MD-02327 JOSEPH R. GOODWIN U.S. DISTRICT JUDGE

EXPERT REPORT OF DR. VLADIMIR IAKOVLEV

I. BACKGROUND

I am an anatomical pathologist and director of Cytopathology at the Department of Laboratory Medicine, St. Michael's Hospital, Toronto, Canada. I hold an appointment at the Department of Laboratory Medicine and Pathobiology, University of Toronto. My professional activities include diagnostic examination of specimens surgically removed from human patients. These are larger excisions, smaller biopsies and cellular aspirations or smears. The organs and sites include genitourinary organs, gastrointestinal, head & neck, pulmonary, soft tissue and bone. My annual practice volume amounts to 3000-5000 cases. As a clinical physician, I provide clinical consultations to physicians at St. Michael's Hospital, which requires me to examine pathology specimens, review clinical information relating to the patient, and reach conclusions about the cause of a patient's injuries or illnesses. As an academic physician, I pursue research endeavors and teach medical students and residents. My academic activities also include tumor boards and teaching at CME workshops. I am also knowledgeable in the areas of chemistry, hematology, microbiology, serology, immunology and other special laboratory studies as they relate to my practice of pathology.

My pathology training was completed at the University of Manitoba Anatomical Pathology residency program, Canada. I hold medical licenses in the province of Ontario, Canada and in the State of Michigan, USA. As a pathologist with a subspecialty in anatomical pathology, I am a fellow of the Royal College of Physicians of Canada and a diplomate of the American Board of Pathology. For research training, I completed the Molecular Oncologic Fellowship Program at the Ontario

across nearly all of the pores. [274] [183] It also provides a rigid connection between the composite mesh-scar structure and the surrounding normal tissue.

Polypropylene degradation

For nearly a half century, scientists around the world have studied polypropylene, including Ethicon's Prolene used in TVT product and have consistently found that polypropylene degrades over time after being implanted in the body. [386] [229] [110] [102] [112] [529] [337] [271] [467] [247] [431] [448] [64] [310] [556].

For example, dating back to the 1970s, Liebert *et al.* found that polypropylene will degrade *in vivo* over time if not adequately protected by antioxidants. [310] In 1998, Prolene was compared to another polymer called PVDF in an animal study.[337] The researchers found that explanted Prolene degraded after 1 and 2 years, while PVDF remained intact. Similarly, later studies also found that surgical polypropylene mesh will degrade over time after implantation in the human body.[110][102][529] [556] Environmental stress and oxidative degradation facilitated by macrophages have been found to be the most likely mechanisms to explain *in vivo* degradation of polypropylene. [60] [337] [386] [229] [110] [102] [112] [529] [337] [271] [467] [247] [431] [448] [64] [310] [556].

Recently, degradation of polypropylene was detected using histological and transmission electron microscopy approaches [211] [215] [216] [556]. This was observed using a combination of histological stains in regular and polarized light. Polarized light microscopy has been reliably used for nearly 100 years to describe the characteristics of explanted foreign materials. [470] As demonstrated by Ethicon's internal documents, the histological methods have been used by Ethicon's scientists to determine whether Prolene degrades in vivo. The findings lead Ethicon's scientists to conclude that Prolene degrades forming an outer layer of degraded material and the cracking observed on the surface of Prolene by scanning electron microscopy is altered polypropylene and not proteinaceous material. [156] The main feature of degradation is cracking of the polypropylene surface [386] [229] [110] [102] [112] [529] [556]. Similar process occurs outside of body. [467] [247] [431] As a result, the material loses tensile strength and becomes brittle. Loss of mechanical properties was shown in explanted meshes. [448] Cracking also indicates that there are internal forces acting to shrink and deform the material. In relation to clinical symptoms, degradation needs to be considered as a factor of additional stiffening and late deformations of the mesh, independent of stiffening and deformations related to scar

maturation, ingrown scar contraction, mesh folding/multilayering. An important conclusion should be made that if chemical and physical properties of a material change while it is in the body it should not be used for permanent applications and for anatomical sites from which the devices cannot be safely removed. There should be planned exit strategies for complete and safe device removal and with minimal residual tissue damage.

The literature also includes a much smaller number of publications that question whether polypropylene fibers degrade in vivo. [467] [247] [558] The alternative hypotheses were that the cracking either occurs within a proteinaceous layer (i.e., biologic) or was caused by sample preparation (e.g., drying, formalin or chemical reagents used to clean the explanted material prior to examination). Ethicon's experts have similarly espoused in prior cases that a protein-formaldehyde polymer forms around the mesh fibers while the mesh is being stored in formalin. The hypothesis has not been proven and Ethicon's own scientists made conclusions disproving this hypothesis. The hypothesis is not viable since there are multiple features disproving it: the degradation layer retains premanufactured dye granules and optical properties of polypropylene, is can melt and meld with non-degraded polypropylene, cracking of the mesh fibers can be observed immediately after the mesh is removed from the body, the degradation layer does not form around some other implantable materials (GoreTex, polyester), its thickness correlates with time in the body but with time of storage.[556] Also, testing of polypropylene by multiple manufacturers indicates that it is resistant to formalin, which contradicts the theories that exposure to formalin causes polypropylene to degrade. [555]

Review of Ethicon's internal documents

In addition to my review of the peer-reviewed publications, I have also reviewed internal Ethicon documents and the deposition of an Ethicon scientist, Dr. Thomas Barbolt. Ethicon's internal documents and the testimony of Dr. Barbolt provide further evidence that the Prolene will degrade over time after implantation in the human body.

In 1983, Ethicon's scientists used nearly identical methods used by me to determine whether Prolene degrades *in vivo*, including histological preparations, light microscopy, and polarized light. [156] Like my own studies discussed herein, Ethicon's scientists found that Prolene degrades and cracks after implantation in the human body. Interestingly, just as I found in this and other mesh explants, Ethicon's scientists opined that "the cracked layer appeared blue in gross specimens and blue dye particles were evident in histological sections of the layer. This

mesh migration and the breakdown of the overlying mucosa. Mesh migration is discussed in #15. The mucosal breakdown can have complex mechanisms where infection, vascular supply, tissue mobility, size and depth of the mesh device and other factors can play roles. Images of mucosal erosion are shown in Figure set 11.

18. **Acute inflammation due to mucosal erosion.** Mucosal erosion of the transvaginal Ethicon mesh becomes a chronic open wound and an entry for infectious organisms. This is associated with acute inflammation and formation of granulation tissue. Fragile granulation tissue produces discharge and bleeds easily. Presence of bacterial infection triggers acute inflammatory response which becomes superimposed on the earlier described chronic non-specific and foreign body type inflammation. Examples of superimposed acute inflammation are shown in Figure set 12. This additional inflammation plays role in tissue damage and further stimulus for pain receptors.
19. **Polypropylene degradation.** Microscopic examination of explanted Ethicon mesh confirms what has been reported otherwise in the medical and scientific literature: polypropylene degrades *in vivo*. Examination reveals a polypropylene degradation layer on the outermost layer of the mesh filaments. The layer differs from the non-degraded core by its ability to trap histological dyes in the nanocavities produced in polypropylene due to degradation. At the same time the degraded material retains inclusions (blue granules) and optical properties (birefringence in polarized light) of polypropylene. Figure set 13 shows representative images of the degradation layer in explanted Ethicon transvaginal mesh devices.
20. **Absence of degradation after exposure to formalin and chemicals of tissue processing.** Polypropylene of pristine polypropylene mesh, including Prolene does not degrade due to exposure to formalin. This has been shown in my experiments and texting by several manufacturers. Examples of mesh after exposure to formalin up to 4 month followed by routine tissue processing are shown in Figure set 14.
21. **Gradual growth of the degraded year over the years in the body.** The degraded layer on an implanted polypropylene mesh, including Prolene accumulates gradually over the years in the body. See Figure 15. As a result, the mechanical properties of the mesh fibers change. The degraded layer cracks indicating its brittleness. As in many brittle porous materials brittleness and porosity are not exclusive of each other.
22. **Cracking of degraded layer observed immediately after mesh removal from the body.** The cracked degradation layer can be visible immediately after excision See Figure

16. The claims that the cracked layer is dried biofilm-proteins or formalin-protein polymer are unsubstantiated since cracking can be seen before the proteins could dry or be cross-linked by formalin.

23. **Melting of degraded polypropylene due to surgical cautery.** The degraded layer shows sites of melting occurred during the use of surgical cautery during excision. This finding confirms that the degraded layer was present before the excision surgery and formed in the body. The bark mixes with the non-degraded core while melting which confirms that it is compatible with the core polypropylene. The feature is shown in Figure set 17.
24. **Absence of stainable layer on non-polypropylene implantable polymers**. In cases when polypropylene mesh was secured by non-polypropylene permanent sutures the non-polypropylene materials do not show formation of a stainable outer layer. If the layer was formed by body proteins it would not have a strict preference to one polymer. See Figure set 18.
25. **Correlation with internal Ethicon documents.** Based on the features described in opinions 16-23, review of the body of scientific literature, review of Ethicon's internal documents and internal studies, it is my opinion that Prolene polypropylene used by Ethicon degrades *in vivo*. Figure sets 19.
26. **Degenerative calcifications can form** triggered by the mesh related pathological tissue changes.The calcific deposits are different from degraded polypropylene. In cases were the mesh migrates into the bladder these calcifications can grow to larger bladder stone.
27. **Mesh excision cannot restore pre-existent tissue state.** Mesh placement causes tissue damage, then while in the body the mesh induces scarring, contracts and migrates expanding the zone of tissue damage. An excision either removes the mesh and all surrounding scarred/damaged tissue leaving a larger defect, or partially removes the scar plate leaving a smaller defect but with a larger amount of remaining scar. In either scenario the defect needs to heal through scarring. Additionally, in many cases mesh cannot be removed in its entirety, especially from the transobturator and other difficult to access locations.

I reserve the right to supplement this report if new information becomes available.

Sincerely,

Vladimir Iakovlev, MD, FRCPC, FCAP DATE: January 29, 2016

FEES

My billing rate is $475/hr.

LISTING OF CASES IN WHICH TESTIMONY HAS BEEN GIVEN IN THE LAST FOUR YEARS

Lisa Marie Fontes, et al. v. American Medical Systems, Inc.; 2:12-CV-02472

Debbie Jilovec, et al., v. American Medical Systems, Inc.; 2:12-CV-05561

Joann Serrano, v. American Medical Systems, Inc.; 2:12-CV-3719

Mary Weiler, et al. v. American Medical Systems, Inc.; 2:12-CV-05836

Carolyn F. Smothers v. Boston Scientific Corp. ; 2:12-cv-08016

Katherine L. Hall v. Boston Scientific Corp. ; 2:12-cv-08186

Julia Wilson v. Boston Scientific Corp. ; 2012-02626

Ronda Orozco, et al., v. Boston Scientific Corp. ; 2012-03068

Maria Cardenas v. Boston Scientific Corp. ; 2012-02912

Diane Albright v. Boston Scientific Corp. ; 2012-00909

Deborah Barba v. Boston Scientific Corp.